PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 2031002PC/ko	FOR FURTHER ACTION	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
International application No. PCT/FI 2004/000540	International filing date *(day/month/year)* 15 Sept 2004	(Earliest) Priority Date *(day/month/year)* 15 Sept 2003
Applicant Fit Biotech OYJ PLC et al		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 5 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**
   a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
      [ ] The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
   b. [ ] With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. [ ] **Certain claims were found unsearchable** (see Box No. II)

3. [ ] **Unity of invention is lacking** (see Box No. III)

4. With regard to the **title**,
   [ ] the text is approved as submitted by the applicant.
   [X] the text has been established by this Authority to read as follows:

   Selection system containing non-antibiotic resistance selection marker.

5. With regard to the **abstract**,
   [ ] the text is approved as submitted by the applicant.
   [X] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings**,
   a. the figure of the drawings to be published with the abstract is Figure No. _____
      [ ] as suggested by the applicant.
      [ ] as selected by this Authority, because the applicant failed to suggest a figure.
      [ ] as selected by this Authority, because this figure better characterizes the invention.
   b. [X] none of the figures is to be published with the abstract.

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Box No. I **Nucleotide and/or amino acid sequence(s) (Continuation of item1.b of the first sheet)**

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:

   a. type of material

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material

   ☐ in written format

   ☒ in computer readable form

   c. time of filing/furnishing

   ☐ contained in the international application as filed

   ☒ filed together with the international application in computer readable form

   ☐ furnished subsequently to this Authority for the purposes of search

2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

Box No. IV Text of the abstract (Continuation of item 5 of the first sheet)

A selection system free of antibiotic resistance genes, which is based on the use of an araD gene as a selection marker carried on a vector which is inserted in a bacterial strain deficient of the araD gene. The araD gene from E. coli encodes the L-ribulose-5-phosphate-4-epimerase. A method of selecting the cells transformed with a plasmid, which contains the araD gene. The non-antibiotic selection marker makes the system suitable for producing theraputics. The araD gene is not essential for growth of the host but manipulation of it affects the growth under certain selective conditions. Deletion of araD leads to accumulation of substance which is toxic to the host but not to humans. The araD gene is relatively small and therefore a small plasmid may be constructed, which requires less energy for replication, and leads to increased growth rate and yield.

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A. CLASSIFICATION OF SUBJECT MATTER

IPC7: C12N 15/70, C12N 15/61
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC7: C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

WPI, EPO-INTERNAL, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Protein Science, Volume 4, 1995, Arnold Andersson et al, "Purification and preliminary X-ray crystallographic studies of recombinant L-ribulose-5-phosphate 4-epimerase from Escherichia coli" pages 1648-1650, page 1648, column 2, paragraph 2-3, abstract	8
Y	--	9-12
Y	WO 02090558 A1 (FIT BIOTECH OYJ PLC), 14 November 2002 (14.11.2002), (cited in the application, abstract	9-12
	--	

[X] Further documents are listed in the continuation of Box C. [X] See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
18 January 2005	20 -01- 2005
Name and mailing address of the ISA/ Swedish Patent Office Box 5055, S-102 42 STOCKHOLM Facsimile No. +46 8 666 02 86	Authorized officer IDA CHRISTENSEN/BS Telephone No. +46 8 782 25 00

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International application No.
PCT/FI 2004/000540

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Carcinogenesis, Volume 14, No. 2, 1993, Rafael R. Ariza et al, "A method for selection of forward mutations in supF gene carried by shuttle-vector plasmids", pages 303-305, page 303, column 2, paragagraph 3, table 1	13-15
A	PNAS, Volume 97, No. 12, June 2000, Kirill A. Datsenko et al, "One-step inactivation of chromosomal genes in Escherichia coli K-12 using PCR products", pages 6640-6645, abstract	1-24
A	Journal of Bacteriology, Volume 172, No. 11, November 1990, Marta Herrero et, "Transposon Vectors Containing Non-Antibiotic Resistance Selection Markers for Cloning and Stable Chromosomal Insertion of Foreign Genes in Gram-Negative Bacteria', pages 6557-6567, abstract	1-24
A	Journal of Bacteriology, Volume 84, 1962, E. Englesberg et al, "L-Arabinose-sensitive, L-ribulose 5-phosphate 4-epimerase-deficient mutants of Escherichia coli", pages 137-146, abstract	13-21

WO	02090558	A1	14/11/2002	AP	200302914	D	00/00/0000
				BR	0209416	A	30/03/2004
				CA	2446260	A	14/11/2002
				CZ	20033201	A	12/05/2004
				EE	200300483	A	15/04/2004
				EP	1390516	A	25/02/2004
				FI	20010922	A	04/11/2002
				HU	0304053	A	29/03/2004
				JP	2004533247	T	04/11/2004
				SK	14692003	A	07/07/2004
				US	20030129169	A	10/07/2003